

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
US Department of Commerce  
United States Patent and Trademark  
Office, PCT  
2011 South Clark Place Room  
CP2/5C24  
Arlington, VA 22202  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 13 March 2001 (13.03.01)	
International application No. PCT/EP00/06943	Applicant's or agent's file reference FP/VB 59.814
International filing date (day/month/year) 05 July 2000 (05.07.00)	Priority date (day/month/year) 13 July 1999 (13.07.99)
Applicant NASSIF, Xavier et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

19 January 2001 (19.01.01)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Claudio Borton
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

# INTERNATIONAL SEARCH REPORT

Inte Application No  
PCT/EP00/06943

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/22 C12N15/31 C07K16/12 C12N15/10 A61K39/095  
G01N33/53

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, STRAND, BIOSIS, MEDLINE, PASCAL

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NASSIF X ET AL: "What do we know about the entry of Neisseria meningitidis into the meninges?" BULL. INS.PASTEUR, vol. 95, no. 4, 1997, page 219-235 XP004108359 ISSN: 0223-5234 the whole document ---	1
X	WO 92 03467 A (UNIV NORTH CAROLINA) 5 March 1992 (1992-03-05) page 9, line 1 -page 11, line 16 page 21, line 5 -page 23, line 13 --- -/--	1

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

12 January 2001

Date of mailing of the international search report

12. 1. 01

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Mateo Rosell, A.M.

# INTERNATIONAL SEARCH REPORT

Intr      Application No  
PCT/E      00/06943

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ALA'ALDEEN D A A: "VACCINES AGAINST NEISSERIA MENINGITIDIS: PAST, PRESENT AND FUTURE" BIOTECNOLOGIA APLICADA, vol. 13, no. 1, 1996, page 1-7 XP002052679 ISSN: 1027-2852 page 3, paragraph 3 -page 6, last paragraph ---	1
X	GOMEZ J A ET AL: "Antigenicity, cross-reactivity and surface exposure of the Neisseria meningitidis 37 kDa protein (Fbp)" VACCINE, vol. 14, no. 14, 1996, page 1340-1346 XP004070969 ISSN: 0264-410X the whole document ---	1
X	WO 90 06696 A (RIJKINSINSTITUUT VOOR VOLKSGEZ ;PRAXIS BIOLOG INC (US)) 28 June 1990 (1990-06-28) abstract Y page 3, last paragraph -page 4, paragraph 1 page 5, last paragraph -page 6, paragraph 1; examples 1-6,16,17 ---	1 1-24
Y	SARKARI J. ET AL.,: "Variable expression of the Opc outer membrane protein in Neisseria meningitidis is caused by size variation of a promoter containing poly-citidine" MOLECULAR MICROBIOLOGY, vol. 13, no. 2, 1994, pages 207-217, XP000863030 cited in the application the whole document ---	1-24
Y	MAIDEN M.C.J. ET AL.,: "Multilocus sequence typing: a portable approach to the identification of clones within populations of pathogenic microorganisms" PROC. NATL. ACAD. SCI. USA, vol. 95, March 1998 (1998-03), pages 3140-3145, XP002125131 cited in the application the whole document --- -/--	1-24

## INTERNATIONAL SEARCH REPORT

Inte Application No

PCT/ 00/06943

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WATARAI M. ET AL.,: "Disulfide oxidoreductase activity of Shigella flexneri is required for release of Ipa proteins and invasion of epithelial cells."  PROC. NATL. ACAD. SCI. U.S.A.,  vol. 92, 1995, page 4927-4931 XP000857645  the whole document</p> <p>---</p>	1-24
A	<p>PEEK J.A. AND TAYLOR R.K.:  "Characterization of a periplasmic thiol:disulfide interchange protein required for the functional maturation of secreted virulence factors of Vibrio cholerae"  PROC. NATL. ACAD. SCI. U.S.A.,  vol. 89, 1992, page 6210-6214 XP000857644  the whole document</p> <p>---</p>	1-24
A	<p>JONSON G ET AL.,: "Cloning an sequencing of Vibrio cholera mannose-sensitive haemagglutinin pilin gene: localization of mshA within a cluster of type 4 pilin genes"  MOLECULAR MICROBIOLOGY,  vol. 13, no. 1, 1994, pages 109-118,  XP000884514  abstract; figure 1  page 115, left-hand column, paragraph 4  -right-hand column, last paragraph</p> <p>---</p>	1
A	<p>WO 90 04641 A (UNIV LELAND STANFORD JUNIOR ;SCLAVO SPA) 3 May 1990 (1990-05-03)  abstract  page 2, line 1 -page 5, line 23  page 12, line 30 -page 21, line 17  page 41, line 1 -page 44, line 23</p> <p>---</p>	1-24
X	<p>WO 97 28273 A (NORTH AMERICAN VACCINE INC)  7 August 1997 (1997-08-07)  abstract  page 3, line 7 -page 8, line 14; examples 1-5</p> <p>---</p>	1
X	<p>VAN DER LEY P ET AL: "Construction of Neisseria meningitidis strains carrying multiple chromosomal copies of the porA gene for use in the production of a multivalent outer membrane vesicle vaccine"  VACCINE,  vol. 13, no. 4, 1995, page 401-407  XP004057740  ISSN: 0264-410X  the whole document</p> <p>---</p>	1
	<p>---</p> <p>-/--</p>	

# INTERNATIONAL SEARCH REPORT

Inte Application No  
PCT/00/06943

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>SCHEUERPFUG I ET AL.,: "Roles of PilC and PilE proteins in pilus-mediated adherence of Neisseria gonorrhoea and Neisseria meningitidis to human erythrocytes and endothelial and epithelial cells" INFECTION AND IMMUNITY, vol. 67, no. 2, February 1999 (1999-02), pages 834-843, XP000877194 page 834 page 841, left-hand column ---</p>	1-24
A	<p>STIBITZ S ET AL.,: "Genetic analysis of a region of the Bordetella pertussis chromosome encoding filamentous hemagglutinin and the pleiotropic regulatory locus vir" JOURNAL OF BACTERIOLOGY, vol. 170, no. 7, July 1988 (1988-07), pages 2904-2913, XP000884520 page 2904 page 2911 -page 2912 ---</p>	1-24
A	<p>VIRJI M ET AL: "VARIATIONS IN THE EXPRESSION OF PILI: THE EFFECT ON ADHERENCE OF NEISSERIA MENINGITIDIS TO HUMAN EPITHELIAL AND ENDOTHELIAL CELLS" MOLECULAR MICROBIOLOGY, GB, OXFORD, vol. 6, no. 10, 1992, page 1271-1279 XP000560443 the whole document ---</p>	1
A	<p>ZHOU J ET AL: "SEQUENCE DIVERSITY WITHIN THE ARGF, FBP AND RECA GENES OF NATURAL ISOLATES OF NEISSERIA MENINGITIDIS: INTERSPECIES RECOMBINATION WITHIN THE ARGF GENE" MOLECULAR MICROBIOLOGY, vol. 6, no. 15, 1992, page 2135-2146 XP000645119 page 2137, left-hand column, last paragraph -page 2137, right-hand column, paragraph 2 page 2139, left-hand column, paragraph 2 -page 2139, right-hand column, paragraph 1 page 2142, left-hand column, last paragraph --- -/--</p>	1

# INTERNATIONAL SEARCH REPORT

Inte Application No  
PCT/EP 00/06943

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>BARENKAMP S J ET AL: "CLONING, EXPRESSION, AND DNA SEQUENCE ANALYSIS OF GENES ENCODING NONTYPEABLE HAEMOPHILUS INFLUENZAE HIGH-MOLECULAR-WEIGHT SURFACE-EXPOSED PROTEINS RELATED TO FILAMENTOUS HEMAGGLUTININ OF BORDETELLA PERTUSSIS"</p> <p>INFECTION AND IMMUNITY,US,AMERICAN SOCIETY FOR MICROBIOLOGY. WASHINGTON, vol. 60, no. 4, 1 April 1992 (1992-04-01), page 1302-1313 XP000578343 ISSN: 0019-9567 abstract</p>	1
A	<p>--- SALIT IE AND MORTON G: "Adherence of Neisseria meningitidis to human epithelial cells"</p> <p>INFECTION AND IMMUNITY, vol. 31, no. 1, January 1981 (1981-01), pages 430-435, XP000877193 the whole document</p>	1
X	<p>--- EMBL databases; Heidelberg, Germany 18-05-99 AC = AF121772. Neisseria meningitidis NatD (natD) and NatC (natC) genes, complete cds. From nt 1714-3117 XP002156086 abstract</p>	1-24
A	<p>--- WO 94 05326 A (UNIV SASKATCHEWAN) 17 March 1994 (1994-03-17) page 7, line 15 -page 8, line 20 page 12, line 1 -page 28, line 7; example 5</p>	1-24
A	<p>--- STONE BARBARA J ET AL: "Salmonella enteritidis has a homologue of tolC that is required for virulence in BALB/c mice."</p> <p>MOLECULAR MICROBIOLOGY, vol. 17, no. 4, 1995, pages 701-712, XP000978140 ISSN: 0950-382X the whole document</p> <p>-----</p>	1-24

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP 00/06943

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  
1-24
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-24, all partially

Isolated polypeptides/polynucleotides as provided in SEQ.IDs. N.1-26, corresponding to the DsbA ORF (alleles 1-4) from *Neisseria meningitidis* polynucleotides and their corresponding encoded polypeptides.

2. Claims: 1-24, all partially

Isolated polypeptides/polynucleotides as provided in SEQ.IDs. N.27 and 28, corresponding to the FhaB ORF from *Neisseria meningitidis* polynucleotide and its corresponding encoded polypeptide.

3. Claims: 1-24, all partially

Isolated polypeptides/polynucleotides as provided in SEQ.IDs. N.29-52, corresponding to the FhuA ORF from *Neisseria meningitidis* polynucleotides and their corresponding encoded polypeptides.

4. Claims: 1-24, all partially

Isolated polypeptides/polynucleotides as provided in SEQ.IDs. N.53 and 54, corresponding to the Rni5 ORF from *Neisseria meningitidis* polynucleotides and its corresponding encoded polypeptides.

5. Claims: 1-24, all partially

Isolated polypeptides/polynucleotides as provided in SEQ.IDs. N.55-64, corresponding to the Rth17-Rth21 ORF from *Neisseria meningitidis* polynucleotides and their corresponding encoded polypeptides.

6. Claims: 1-24, all partially

Isolated polypeptides/polynucleotides as provided in SEQ.IDs. N.65-90, corresponding to the TolC ORF (alleles 1-3) from *Neisseria meningitidis* polynucleotides and their corresponding encoded polypeptides.



## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>FP/VB 59.814</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/EP 00/ 06943</b>	International filing date (day/month/year) <b>05/07/2000</b>	(Earliest) Priority Date (day/month/year) <b>13/07/1999</b>
Applicant <b>INSTITUT NATIONAL DE LA SANTE ET DE ...</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.  
☒ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

**NEISSERIA MENINGITIDIS COMPOUNDS AND ANTI-INFECTION APPLICATIONS THEREOF**

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

Intr Application No

PCT/00/06943

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9203467 A	05-03-1992	AU 8747791 A CA 2087958 A EP 0546118 A JP 6500562 T US 5912336 A	17-03-1992 24-02-1992 16-06-1993 20-01-1994 15-06-1999
WO 9006696 A	28-06-1990	NL 8803111 A NL 8900030 A NL 8901612 A AT 120093 T AU 640118 B AU 4821990 A DE 68921895 D DE 68921895 T DK 117491 A EP 0449958 A ES 2070312 T JP 6503465 T NL 8900036 A NO 305463 B CA 2000735 A CA 2007248 A DE 8901378 U DE 68900982 D DK 511389 A EP 0377233 A ES 2029372 T US 5057007 A PT 92807 A,B	16-07-1990 01-08-1990 16-07-1990 15-04-1995 19-08-1993 10-07-1990 27-04-1995 07-09-1995 15-08-1991 09-10-1991 01-06-1995 21-04-1994 16-07-1990 07-06-1999 06-07-1990 06-07-1990 23-03-1989 16-04-1992 07-07-1990 11-07-1990 01-08-1992 15-10-1991 31-07-1990
WO 9004641 A	03-05-1990	AT 176913 T AU 643190 B AU 4515589 A DE 68928933 D DE 68928933 T DK 76191 A EP 0439542 A JP 4501506 T NO 911673 A US 6036960 A	15-03-1999 11-11-1993 14-05-1990 01-04-1999 26-08-1999 14-06-1991 07-08-1991 19-03-1992 26-06-1991 14-03-2000
WO 9728273 A	07-08-1997	AU 2115897 A EP 0877816 A HU 9901039 A NO 983474 A PL 328096 A	22-08-1997 18-11-1998 28-07-1999 30-09-1998 04-01-1999
WO 9405326 A	17-03-1994	AT 173166 T AU 683221 B AU 4939193 A DE 69322092 D DE 69322092 T EP 0659086 A IL 106903 A US 5747309 A	15-11-1998 06-11-1997 29-03-1994 17-12-1998 15-07-1999 28-06-1995 10-01-1997 05-05-1998

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-24, all partially

Isolated polypeptides/polynucleotides as provided in SEQ.IDs. N.1-26, corresponding to the DsbA ORF (alleles 1-4) from *Neisseria meningitidis* polynucleotides and their corresponding encoded polypeptides.

2. Claims: 1-24, all partially

Isolated polypeptides/polynucleotides as provided in SEQ.IDs. N.27 and 28, corresponding to the FhaB ORF from *Neisseria meningitidis* polynucleotide and its corresponding encoded polypeptide.

3. Claims: 1-24, all partially

Isolated polypeptides/polynucleotides as provided in SEQ.IDs. N.29-52, corresponding to the FhuA ORF from *Neisseria meningitidis* polynucleotides and their corresponding encoded polypeptides.

4. Claims: 1-24, all partially

Isolated polypeptides/polynucleotides as provided in SEQ.IDs. N.53 and 54, corresponding to the Rni5 ORF from *Neisseria meningitidis* polynucleotides and its corresponding encoded polypeptides.

5. Claims: 1-24, all partially

Isolated polypeptides/polynucleotides as provided in SEQ.IDs. N.55-64, corresponding to the Rth17-Rth21 ORF from *Neisseria meningitidis* polynucleotides and their corresponding encoded polypeptides.

6. Claims: 1-24, all partially

Isolated polypeptides/polynucleotides as provided in SEQ.IDs. N.65-90, corresponding to the TolC ORF (alleles 1-3) from *Neisseria meningitidis* polynucleotides and their corresponding encoded polypeptides.

PATENT COOPERATION TREATY

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REC'D 16 NOV 2001


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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference FP/VB 59.814		<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP00/06943		International filing date (day/month/year) 05/07/2000	Priority date (day/month/year) 13/07/1999	
International Patent Classification (IPC) or national classification and IPC C07K14/22				
Applicant INSTITUT NATIONAL DE LA SANTE ET DE ...				
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>				
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I <input checked="" type="checkbox"/> Basis of the report</li> <li>II <input type="checkbox"/> Priority</li> <li>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV <input checked="" type="checkbox"/> Lack of unity of invention</li> <li>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI <input type="checkbox"/> Certain documents cited</li> <li>VII <input type="checkbox"/> Certain defects in the international application</li> <li>VIII <input checked="" type="checkbox"/> Certain observations on the international application</li> </ul>				
Date of submission of the demand  19/01/2001		Date of completion of this report  16.11.2001		
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523856 epmu d Fax: +49 89 2399 - 4465		Authorized officer  Page, M  Telephone No. +49 89 2399 7322		



Form PCT/IPEA/409 (cover sheet) (January 1994)

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP00/06943

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-100 as originally filed

**Claims, No.:**

1-24 as originally filed

**Drawings, sheets:**

1/183-183/183 as originally filed

**Sequence listing part of the description, pages:**

1-115 (SEQ ID NOs. 1-116), as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP00/06943

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.  
☒ claims Nos. 1-24 (partialy).

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the said claims Nos. 1-24 (partialy).
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

**IV. Lack of unity of invention**

1. In response to the invitation to restrict or pay additional fees the applicant has:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**International application No. **PCT/EP00/06943**

- ☐ restricted the claims.
- ☒ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- ☐ complied with.
- ☐ not complied with for the following reasons:
4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:
- ☒ all parts.
- ☐ the parts relating to claims Nos. .

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Yes:	Claims	13-24 (partially)
	No:	Claims	1-12 (partially)
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-24 (partially)
Industrial applicability (IA)	Yes:	Claims	1-24 (partially)
	No:	Claims	

**2. Citations and explanations  
see separate sheet****VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP00/06943

The application concerns the provision of a *N. meningitidis* polynucleotide and polypeptide sequences suitable for immunisation purposes.

**Re Item III****Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

III.1 A search report has not been established for **claims 1-24 partially**, particularly to SEQ ID NOs. 29-64, corresponding to Fhu ORF, Rni5 ORF and Rth17-Rth21 ORF.

**Re Item IV****Lack of Unity of Invention**

As laid out in the invitation to pay additional fees, the application is considered to consist of three separate inventions:

**Invention 1: Claims 1-24 (all partially)**

Isolated polypeptides/polynucleotides as provided in SEQ ID NOs. 1-26, corresponding to the DsbA ORF (alleles 1-4) from *N. meningitidis* polynucleotides and their corresponding polypeptides.

**Invention 2: Claims 1-24 (all partially)**

As Invention 1 for SEQ ID NOs. 27 and 28, corresponding to the FhaB ORF.

**Invention 6: Claims 1-24 (all partially)**

As Invention 1 for SEQ ID NOs. 65-90, corresponding to the TolC ORF (alleles 1-3).

**Re Item V****Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement**

V.1 Reference is made to the following documents:



**INTERNATIONAL PRELIMINARY**

International application No. PCT/EP00/06943

**EXAMINATION REPORT - SEPARATE SHEET**

- D1: WO 92 03467 A (UNIV NORTH CAROLINA) 5 March 1992 (1992-03-05)
- D2: ALA'ALDEEN D A A: 'VACCINES AGAINST NEISSERIA MENINGITIDIS: PAST, PRESENT AND FUTURE' BIOTECNOLOGIA APLICADA, vol. 13, no. 1, 1996, page 1-7 XP002052679 ISSN: 1027-2852
- D3: GOMEZ J A ET AL: 'Antigenicity, cross-reactivity and surface exposure of the Neisseria meningitidis 37 kDa protein (Fbp)' VACCINE, vol. 14, no. 14, 1996, page 1340-1346 XP004070969 ISSN: 0264-410X
- D4: WO 90 06696 A (RIJKINSINSTITUUT VOOR VOLKSGEZ ;PRAXIS BIOLOG INC (US)) 28 June 1990 (1990-06-28)
- D5: WO 97 28273 A (NORTH AMERICAN VACCINE INC) 7 August 1997 (1997-08-07)
- D6: EMBL databases; Heidelberg, Germany 18-05-99 AC = AF121772. Neisseria meningitidis NatD (natD) and NatC (natC) genes, complete cds. From nt 1714-3117 XP002156086

**V.2 Novelty - Art.33(1) and (2) PCT:****V.2.1 Invention 1: Claims 1-24 (partially)**

SEQ ID NOs. 1-26, corresponding to the DsbA ORF of N. meningitidis are not anticipated by the prior art. The closest sequence disclosed is P52234, displaying 29% identity over 194 amino acids **Claims 1-24 (partially)** are therefore considered to be novel.

**V.2.2 Invention 2: Claims 1-24 (partially)**

SEQ ID NOs. 27 and 28, corresponding to the FhaB ORF of N. meningitidis are not anticipated by the prior art. The closest sequence disclosed is P12255, displaying 32% identity over 31 amino acids **Claims 1-24 (partially)** are therefore considered to be novel.

**V.2.3 Invention 3: Claims 1-24 (partially)**

SEQ ID NOs. 65-90, corresponding to the TolC ORF of N. meningitidis are anticipated by the sequence AF121772 disclosed in D6. This sequence is identical to SEQ ID NOs. 65, 67 and 71 (99.8%, 99.6% and 100% respectively). The polypeptide sequence is identical. **Claims 1-12 (partially)** therefore lack

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP00/06943

novelty in light of D6. Claim 13-24 (partially), however, appear to be novel.

**V.3 Inventive Step - Art.33(1) and (3) PCT:****V.3.1 Invention 1: Claims 1-24 (partially)**

As SEQ ID NOs. 1-26 are not anticipated by the prior art and the polypeptides thereof appear to have potential as vaccine proteins (Example 2), inventive step is acknowledged for claims 1-24 (partially).

**V.2.2 Invention 2: Claims 1-24 (partially)**

Although the proposed polynucleotide and/or polypeptide sequences SEQ ID NOs. 27 and 28 have not been previously disclosed, there is no worked example demonstrating that the claimed subject matter has the desired function of providing a suitable vaccine for immunisation against N. meningitidis. In order to recognise inventive step, the IPEA is obliged to satisfy itself that the problem underlying an application is indeed solved by the claimed compounds/methods. This requirement is not met by the subject matter of claims 1-24 (partially).

**V.2.3 Invention 3: Claims 1-24 (partially)**

The above objections to inventive step for Invention 2 are applied to Invention 3 mutatis mutandis. Furthermore, the prior art discloses extensively polypeptide which are suitable vaccines against N. meningitidis (see D2-D5). The use of a known polypeptide for immunisation purposes is not considered to demonstrate any inventive step, particularly in the absence of worked examples or comparative data demonstrating any advantages of the protein corresponding to SEQ ID NOs 65-90 over the prior art.

**Re Item VIII****Certain observations on the international application**

VIII.1 Claim 15 is dependent on the host cell of claim 18, which refers to a vaccine composition, rendering claim 15 unclear (Article 6 PCT).

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
18 January 2001 (18.01.2001)

PCT

(10) International Publication Number  
**WO 01/04150 A3**

(51) International Patent Classification<sup>7</sup>: **C07K 14/22**,  
C12N 15/31, C07K 16/12, C12N 15/10, A61K 39/095,  
G01N 33/53

**MERKER, Petra** [DE/DE]; Arkonaplatz 3, 10435 Berlin  
(DE).

(21) International Application Number: **PCT/EP00/06943**

(74) Agents: **PEAUCELLE, Chantal et al.**; Cabinet Armen-  
gaud Ainé, 3, Avenue Bugeaud, F-75116 Paris (FR).

(22) International Filing Date: **5 July 2000 (05.07.2000)**

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ,  
DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,  
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,  
TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(25) Filing Language: **English**

(26) Publication Language: **English**

(30) Priority Data:  
99401764.8 **13 July 1999 (13.07.1999)** EP

(84) Designated States (*regional*): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian  
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European  
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,  
IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG,  
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(71) Applicants (*for all designated States except US*):  
**INSTITUT NATIONAL DE LA SANTE ET DE  
LA RECHERCHE MEDICALE (I.N.S.E.R.M.)**  
[FR/FR]; 101, rue de Tolbiac, F-75654 Paris Cedex  
13 (FR). **MAX-PLANCK-GESELLSCHAFT ZUR  
FÖRDERUNG DES WISSENSCHAFTEN E.V.**  
[DE/DE]; Hofgartenstrasse 2, 80539 Munich (DE).

Published:  
— *with international search report*

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **NASSIF, Xavier**  
[FR/FR]; 1, Square Charles Laurent, F-75015 Paris (FR).  
**TINSLEY, Colin** [FR/FR]; 16, Square Jean Thébaud,  
F-75015 Paris (FR). **KLEE, Silke** [DE/DE]; Isenburger  
Weg 65C, 13591 Berlin (DE). **ACHTMAN, Mark**  
[CA/DE]; Neuenburger Strasse 16, 10969 Berlin (DE).

(88) Date of publication of the international search rep rt:  
**13 December 2001**

*For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.*

(54) Title: **NEISSERIA MENINGITIDIS COMPOUNDS AND ANTI-INFECTION APPLICATIONS THEREOF**

(57) Abstract: The invention provides novel *Neisseria meningitidis* (Nm) polypeptides and polynucleotides which cover the Nm genetic diversity, and which correspond to polypeptide of Nm outer membrane and/or periplasma, and to methods for producing such Nm compounds. Also provided are anti-Nm infection, and particularly diagnostic, prophylactic and therapeutic uses thereof.



**WO 01/04150 A3**